

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of claims:

1-26. (canceled)

27. (currently amended) A method of identifying a gene that affects glucose transport, the method comprising:

- (a) contacting *in vitro* an adipocyte having a cell membrane with an siRNA targeted against the gene, thereby forming a mixture;
- (b) electroporating the mixture under conditions such that the cell membrane becomes permeablized and the siRNA is introduced into the adipocyte;
- (c) culturing the adipocyte cell under conditions suitable for expression of the targeted gene and such that the siRNA mediates RNAi; and
- (d) assaying glucose transport in the adipocyte cell, wherein a modulation in glucose transport indicates that the targeted gene affects glucose transport;

thereby identifying a gene that affects glucose transport.

28-37. (canceled)

38. (currently amended) The method of claim 27 or 79, wherein the electroporation is carried out at between about 0.01 kV and about 2.0 kV, and at between about 350 μ F and about 1550 μ F capacitance.

39. (currently amended) The method of claim 27 or 79, wherein the electroporation is carried out at between about 0.02 kV and about 1.0 kV, and at between about 500 μ F and about 1350 μ F capacitance.

40. (currently amended) The method of claim 27 or 79, wherein the electroporation is carried out at between about 0.05 kV and about 0.5 kV, and at between about 750 μ F and about 1150 μ F capacitance.
41. (currently amended) The method of claim 27 or 79, wherein the electroporation is carried out at between about 0.1 kV and about 0.25 kV, and at between about 850 μ F and about 1050 μ F capacitance.
42. (currently amended) The method of claim 27 or 79, wherein the electroporation is carried out at between about 0.1 kV and about 0.25 kV, and at between about 900 μ F and about 1000 μ F capacitance.
43. (currently amended) The method of claim 27 or 79, wherein the electroporation is carried out at about 0.18 kV and 960 μ F capacitance.
44. (currently amended) The method of claim 27 or 79, wherein the electroporation is carried out at room temperature.
45. (currently amended) The method of claim 27 or 79, wherein glucose transport is assayed at least 12 hours following electroporation.
46. (currently amended) The method of claim 27 or 79, wherein glucose transport is assayed between about 24 and 48 hours following electroporation.
47. (currently amended) The method of claim 27 or 79, wherein increased glucose transport indicates that the targeted gene affects glucose transport.
48. (currently amended) The method of claim 27 or 79, wherein reduced glucose transport indicates that the targeted gene affects glucose transport.
49. (currently amended) The method of claim 27 or 79, wherein glucose transport is assayed by assaying insulin-mediated glucose uptake.

50. (currently amended) The method of claim 27 or 79, wherein glucose transport is assayed by assaying insulin-mediated GLUT4 translocation.
51. (currently amended) The method of claim 27 or 79, wherein the siRNA is sufficiently complementary to the mRNA of the target gene to mediate RNAi
52. (currently amended) The method of claim 27 or 79, wherein the siRNA comprises at least one deoxyribonucleotide or nucleotide analog. ~~is an siRNA derivative.~~
53. (currently amended) The method of claim 52, 27, wherein the siRNA comprising at least one deoxyribonucleotide or nucleotide analog ~~derivative~~ has increased stability relative to an siRNA lacking the at least one deoxyribonucleotide or nucleotide analog.
54. (currently amended) The method of claim 53, wherein the siRNA comprising at least one deoxyribonucleotide or nucleotide analog ~~derivative~~ has increased RNAi activity relative to an siRNA lacking the at least one deoxyribonucleotide or nucleotide analog.
55. (currently amended) The method of claim 53, wherein the siRNA comprising at least one deoxyribonucleotide or nucleotide analog ~~derivative~~ has reduced RNAi activity relative to an siRNA lacking the at least one deoxyribonucleotide or nucleotide analog.
56. (currently amended) The method of claim 27 or 79, wherein the adipocyte is a human adipocyte.
57. (currently amended) The method of claim 27 or 79, wherein the adipocyte is a non-human mammalian adipocyte.
58. (currently amended) The method of claim 27 or 79, wherein the gene is expressed exogenously in the adipocyte.

59. (currently amended) The method of claim 27 or 79, wherein the gene is expressed endogenously in the adipocyte.

60. (withdrawn) A method of identifying a gene that affects glucose transport, the method comprising:

- (a) contacting an adipocyte having a cell membrane with a nucleic acid molecule, wherein the nucleic acid is capable of expressing an siRNA targeted against the gene, thereby forming a mixture;
- (b) electroporating the mixture under conditions such that the cell membrane becomes permeabilized and the nucleic acid molecule is introduced into the adipocyte;
- (c) culturing the cell under conditions suitable for expression of the targeted gene and the siRNA, and under conditions such that the siRNA mediates RNAi; and
- (d) assaying glucose transport in the cell, wherein a modulation in glucose transport indicates that the targeted gene affects glucose transport;

thereby identifying a gene that affects glucose transport.

61. (withdrawn) The method of claim 60, wherein the electroporation is carried out at between about 0.01 kV and about 2.0 kV, and at between about 350 μ F and about 1550 μ F capacitance.

62. (withdrawn) The method of claim 60, wherein the electroporation is carried out at between about 0.02 kV and about 1.0 kV, and at between about 500 μ F and about 1350 μ F capacitance.

63. (withdrawn) The method of claim 60, wherein the electroporation is carried out at between about 0.05 kV and about 0.5 kV, and at between about 750 μ F and about 1150 μ F capacitance.

64. (withdrawn) The method of claim 60, wherein the electroporation is carried out at between about 0.1 kV and about 0.25 kV, and at between about 850 μ F and about 1050 μ F capacitance.

65. (withdrawn) The method of claim 60, wherein the electroporation is carried out at between about 0.1 kV and about 0.25 kV, and at between about 900 μ F and about 1000 μ F capacitance.

66. (withdrawn) The method of claim 60, wherein the electroporation is carried out at about 0.18 kV and 960 μ F capacitance.

67. (withdrawn) The method of claim 60, wherein the electroporation is carried out at room temperature.

68. (withdrawn) The method of claim 60, wherein glucose transport is assayed at least 12 hours following electroporation.

69. (withdrawn) The method of claim 60, wherein glucose transport is assayed between about 24 and 48 hours following electroporation.

70. (withdrawn) The method of claim 60, wherein increased glucose transport indicates that the targeted gene affects glucose transport.

71. (withdrawn) The method of claim 60, wherein reduced glucose transport indicates that the targeted gene affects glucose transport.

72. (withdrawn) The method of claim 60, wherein glucose transport is assayed by assaying insulin-mediated glucose uptake.

73. (withdrawn) The method of claim 60, wherein glucose transport is assayed by assaying insulin-mediated GLUT4 translocation.

74. (withdrawn) The method of claim 60, wherein the siRNA is sufficiently complementary to the mRNA of the targeted gene to mediate RNAi

75. (withdrawn) The method of claim 60, wherein the adipocyte is a human adipocyte.

76. (withdrawn) The method of claim 60, wherein the adipocyte is a non-human mammalian adipocyte.

77. (withdrawn) The method of claim 60, wherein the targeted gene is expressed exogenously in the adipocyte.

78. (withdrawn) The method of claim 60, wherein the targeted gene is expressed endogenously in the adipocyte.

79. (currently amended) A method of identifying a gene involved in an insulin response disease or disorder, the method comprising:

- (a) contacting *in vitro* an adipocyte having a cell membrane with an siRNA targeted against the gene, thereby forming a mixture;
- (b) electroporating the mixture under conditions such that the cell membrane becomes permeablized and the siRNA is introduced into the adipocyte;
- (c) culturing the adipocyte cell under conditions suitable for expression of the targeted gene and such that the siRNA mediates RNAi; and
- (d) assaying glucose transport in the adipocyte cell, wherein a modulation in glucose transport indicates that the targeted gene is involved in an insulin response disease or disorder;

thereby identifying a gene that is involved in an insulin response disease or disorder.

80. (withdrawn) A method of identifying a gene involved in an insulin response disease or disorder, the method comprising:

- (a) contacting an adipocyte having a cell membrane with a nucleic acid molecule, wherein the nucleic acid is capable of expressing an siRNA targeted against the gene, thereby forming a mixture;
- (b) electroporating the mixture under conditions such that the cell membrane becomes permeablized and the nucleic acid molecule is introduced into the adipocyte;

- (c) culturing the cell under conditions suitable for expression of the targeted gene and the siRNA, and under conditions such that the siRNA mediates RNAi; and
- (d) assaying glucose transport in the cell, wherein a modulation in glucose transport indicates that the targeted gene is involved in an insulin response disease or disorder; thereby identifying a gene involved in an insulin response disease or disorder.

81. (original) The method of claim 79 or 80, wherein the disease or disorder is selected from the group consisting of Type II diabetes, insulin resistance and obesity.

82. (new) The method of claim 27 or 79, wherein the mixture comprises 0.1 – 80 nmole siRNA and 1-10 million adipocytes.

83. (new) The method of claim 27 or 79, wherein the mixture comprises about 20 nmole siRNA and about 5×10^6 adipocytes.

84. (new) A method of identifying a gene that affects glucose transport, the method comprising:

- (a) contacting *in vitro* an adipocyte having a cell membrane with an siRNA targeted against the gene, thereby forming a mixture, wherein the mixture comprises 0.1 – 80 nmole siRNA and 1-10 million adipocytes;
- (b) electroporating the mixture under conditions such that the cell membrane becomes permeabilized and the siRNA is introduced into the adipocyte, wherein the electroporation is carried out at between about 0.01 kV and about 2.0 kV, and at between about 350 μ F and about 1550 μ F capacitance;
- (c) culturing the adipocyte under conditions suitable for expression of the targeted gene and such that the siRNA mediates RNAi; and
- (d) assaying glucose transport in the adipocyte, wherein a modulation in glucose transport indicates that the targeted gene affects glucose transport; thereby identifying a gene that affects glucose transport.

85. (new) A method of identifying a gene involved in an insulin response disease or disorder, the method comprising:

- (a) contacting *in vitro* an adipocyte having a cell membrane with an siRNA targeted against the gene, thereby forming a mixture, wherein the mixture comprises 0.1 – 80 nmole siRNA and 1-10 million adipocytes;
- (b) electroporating the mixture under conditions such that the cell membrane becomes permeablized and the siRNA is introduced into the adipocyte, wherein the electroporation is carried out at between about 0.01 kV and about 2.0 kV, and at between about 350 μ F and about 1550 μ F capacitance;
- (c) culturing the adipocyte under conditions suitable for expression of the targeted gene and such that the siRNA mediates RNAi; and
- (d) assaying glucose transport in the adipocyte, wherein a modulation in glucose transport indicates that the targeted gene is involved in an insulin response disease or disorder; thereby identifying a gene that is involved in an insulin response disease or disorder.